Homologous recombination in human embryonic stem cells: a tool for advancing cell therapy and understanding and treating human disease.

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Public Summary:
Human Embryonic Stem cells (hESCs) are undifferentiated cells that can generate all the cells in the body. Many investigators are trying to generate specific types of cells to treat specific types of human disorders, ushering in a new era of treatments for various diseases. One obstacle to this goal is the difficulty in generating specific types of cells from hESCs. To help achieve that goal, investigators are starting to generate reporter cells, which are cells that express an easy to see protein that tells the investigator that the cells they want are in the dish and helps them isolate the cells. These reporter cells are generated using a technique called homologous recombination, or HR. The same technique can also be used to remove a specific gene sequence from the hESC to help the researcher better study and understand the role of a specific gene in the development of a specific cell type. That knowledge can be used to better understand aspects of human development and the development of the cell type(s) of interest. Again, this is achieved using HR. HR was developed and applied using mouse ES cells. Its application to hESCs was not easy, and for years many people speculated that it could not be achieved. However, new work by various scientists have shown that HR can be performed in hESCs, and the potential of this technique is large. This paper reviews the literature to date related to HR in hESCs and provides lots of summary information to help others begin to incorporate this exciting technique into their research efforts.

Scientific Abstract:
Human embryonic stem cells (hESCs) hold great promise for ushering in an era of novel cell therapies to treat a wide range of rare and common diseases, yet they also provide an unprecedented opportunity for basic research to yield clinical benefit. HESCs can be used to better understand human development, to model human diseases, to understand the contribution of specific mutations to the pathogenesis of disease, and to develop human cell-based screening systems to identify novel therapeutic agents and evaluate potential toxicity of therapeutic agents under development. Such basic research will benefit greatly from efficient methods to perform targeted gene modification, an area of hESC investigation that is currently in its infancy. Moreover, the reality of hESC-based cellular therapies will require improved methods for generating the specific cells of interest, and reporter cell lines generated through targeted gene modifications are expected to play an important role in developing optimal cell-specific differentiation protocols. Herein, we review the current status of homologous recombination in hESCs, a gene targeting technique that is sure to continue to improve, and to play an important role in realizing the maximal human benefit from hESCs.